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09/043,944	10/06/2000	Iva Greenwald	48231-A-PCT	7588

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John P White
Cooper & Dunham
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 07/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/043,944	GREENWALD ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6 December 2000 (Paper No. 11)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☒ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 65* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 65* is/are rejected.

7)☒ Claim(s) *1,2,14,16 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12, 13 & 17
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' preliminary amendment filed 6 December 2000 (Paper No. 11) as to amendment of claims 7, 10, 12 and 15-19 and cancellation of claims 22-64 and 66-86, and applicants' request for extension of time of one month filed 6 December 2000 (Paper No. 9) have been entered. Thus, claims 1-21 and 65 are pending and under examination examined in this Office action.

Objection to Specification/Claims

The disclosure is objected to because of the following informalities:

(1) In page 14, line 35, "RT-PCR" should be spelled out in full for the first instance of use.

(2) In page 15, line 4 and 5, "SEQ. ID. 7" and "SEQ. ID. 8" should be changed to "SEQ ID NO:7" and "SEQ ID NO:8", respectively.

(3) In page 252, lines 35 and 36, the specification recites "oligonucleotide sequences in the absence of "SEQ ID NO:_" for the sequences. There are no corresponding sequences in the paper copy of the sequencing listing. See 37 C.F.R. 1.821. Correction is required. A new paper copy and a computer readable from (CRF) are required as is the statement regarding no new matter and that the paper and CRF copies are identical. The period for response this objection is the same as the period for response to this Office action and runs from the mailing date of this Office action. See also the nucleotide sequences in page 53, lines 12-14, 20-21 and 29-32, and, page 54, lines 1-3 and 15-16.

(4) In pages 4-6, the specification sets forth a brief description of drawings (Figures 1-3) absent the corresponding figures.

(5) Claims 1 and 2 are objected to as non-compliant with 37 C.F.R. 1.821 (d). The "SEQ ID NO:_" is missing from the disclosed polynucleotide molecule encoding a SEL-12 polypeptide (claim 1) and a mutated SEL-12 molecule (claim 2).

(6) In claim 14, "an RNA" should be changed to "a RNA".

(7) In claim 16, "a promoter of RNA transcription" should be changed to "a promoter for RNA transcription".

(8) In claim 21 "a" is missing before "plant".

Corresponding correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 12-14 and 65 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claim 12 and its dependent claims thereof and claim 65, as written, do not sufficiently distinguish over other polypeptide, proteins and enzymes as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the

inventor, *e.g.*, by insertion of "recombinantly produced or isolated" (see pages 28-29 of the specification). See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5, 11-14, 20-21 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites "position 115", "position 132", position 215", "position 229", "position 254", "position 255"; "position 255", "position 371", "position 387", "position 104" and "position 204; without recitation as to which SEQ ID NO:_ the positions refer, the position assignments are indefinite. The dependent claims are also rejected.

Claim 4 is unclear as to "one or more alteration"; how many are there the alterations? Are all residues of the SEL-12 polypeptide are mutated? Because the specification does not define "alteration", claim 4 is indefinite as to whether or not the alteration includes chemical modification to the sequence. Additionally, there is not antecedent basis for the recitation "one or more alteration " in claim 2.

Claim 5 recites "... protein that homologous to SEL-12". The recitation is unclear as to whether or not the homolog refers to (i) functional homology, or, (ii) structural homology including homology in folding structure (ternary structure) of protein rather than primary structure (amino acid sequence).

Claim 11 recites "the amino acid sequence show in Figure 1A". Yet. there is no Figure 1A in the current specification but a brief description of drawings of the figure (see page 4 of the PCT/US9615727), which renders the claim indefinite. In addition, claim 11 is indefinite because the claim recites "the amino acid sequence" without setting forth the SEQ ID NO:_ thereof.

Claim 12 recites "a unique sequence" without reciting SEQ ID NO:_ in which the unique sequence resides, the recitation would render the claim indefinite. Additionally, "a unique sequence" is not apparent regarding whether or not the unique sequence refers to a structural or functional motif, or a mutated region of the sequence. Further, claim 12 recites the limitation "the sequence of a nucleic acid molecule". There is no antecedent basis for this limitation in the claim 1 or 2 or 3 from which claim 12 depends. The dependent claims are also rejected.

Claim 20 is unclear regarding whether or not the recitation "a SEL-12 protein" in the claim differs from the protein disclosed (note the article "a" before "SEL-12 protein"), and whether or not the recited protein is a mutated protein (note that claims 20 as written depends from claim 2 where recites "a mutated protein"). The dependent claim is also included in the rejection.

Claim 65 is indefinite as being dependent from the cancelled claims, i.e., claims 62-64, which renders the claim indefinite.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Deposit requirement

Claims 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the claims recite three expression plasmids, pMX8 and p1-1E, without corresponding deposit numbers. Since the expression vectors recited are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification from the restricted microorganism, or as cellularly replicable plasmid forms, otherwise be readily available to the public. If the organism or the plasmids are not so obtainable or available, the requirement of U.S.C. 112 may be satisfied by a deposit of the microorganism or the plasmids.

The applicants have apparently incorporated specific references into the specification does not eliminate the issue of public availability and permanence as the plasmids from which the expression vectors are derived cited in the references and the reference *per se* do not indicate public availability of the starting materials inasmuch as the biological materials motioned in a publication may be proprietary and not publicly available.

The specification does not disclose a repeatable process to obtain the microorganism from which the protein is to have been obtained nor is it apparent that the bacterial strain BCCM-LMBP is readily available to the public. It is noted that the applicants have deposited the microorganism but there is no indication in the specification as to public availability. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strains have been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition releases to the public upon the issuance of a patent and receipt showing the appropriate biological material was received and entered into the depository, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809 applicants may provide assurance of compliance by an affidavit or declaration, or by statement by an attorney of record over his or her signature and registration number indicating that:

a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

b) all restriction upon availability to the public will be irrevocably removed upon granting of the patent;

c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

d) A test of the viability of the biological material at the time the deposit was made and that such test result indicated that said biological material was viable (see 37 C.F.R. 1.807); and

e) the deposit will be replaced if it should ever become unviable.

Claims 7 and 8, which recite the deposit, are rejected under 35 USC 112 first paragraph as lacking adequate written description and enablement for the reason set forth in the rejection to the specification.

Claims 1-17, 20-21 and 65 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated polynucleotide (SEQ ID NO:5) encoding a SEL 12 polypeptide (SEQ ID NO:1). Applicant is not in possession of any polynucleotide encoding SEL-12 polypeptide including (i) splicing variant of SEL-12 as the specification sets forth the DNA is a genomic DNA molecule (see page 7, lines 17-18), (ii) the polynucleotide mutants (variants) encoding SEL-12 mutant encompassing: substitutions, rearrangements, deletions, additions which are generated by in vitro mutagenesis (see page 7,lines 12-13), and (iii) chemically modified polynucleotide sequence (see claim 4 recitation "alteration" which has not been defined in the specification; thus, the alteration would encompass chemical modification).

The isolated nucleic acid encompasses mutations of SEL-12 (see page 7, lines 3-4). There is, however, no the sequence identifier for the claimed polynucleotide nor biological function associate with the claim language (e.g., see claims 1 and 2). Thus, one of ordinary skill in the art would not known which polynucleotide molecule is subject t the mutagenesis in order to produce the claimed "isolated nucleic acid". The instant claim 3 recites mutagenesis in the several positions (e.g., positions 115, 132 and 215 etc.) but does not indicate which polynucleotide sequence on which the mutagenesis is carried out. Without having known what the wild-type sequence is, the skilled artisan therefore would have not been able to practice the claimed invention. Likewise, claim 12 recites "a unique sequence within the sequence of a nucleic acid molecule of claim 1 or 2". In the absence of the SEQ ID NO:_ of the disclosed polynucleotide sequence, undue experimentation is required for the skilled artisan to sort out and characterize the unique sequence in an unidentified polynucleotide.

The specification provides no working examples and guidance as to how to make bioactive variants without being deviated from a core motif structure. The current application describes mutations of presenilins (PS1 and PS2) (see pages 34 and 50) and compares SEL-12 to the presenilins thereof. Yet, in the absence of factual indicia of using the isolated SEL-12 or a representative of SEL-12 variants to characterize the activity thereof, the comparison SEL-12 or variants thereof to the homolog presenilin is an insufficient description for the claimed polynucleotide sequence. Hence, applicants are not in possession of *Sel*-12 mutant (variant) sequence.

Applicant has disclosed only the *name* of *Sel*-12 polynucleotide without reciting the corresponding SEQ ID NO:_ ; therefore, the skilled artisan cannot envision all the contemplated polypeptide sequence possibilities (wild-type along with the variants) recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5,

20001, see especially page 1106 3rd column). Further, the specification fails to describe additional representative species of polynucleotide and variant(s) therefore as mentioned above.

Given the lack of a written description of *any* additional representative species comprising one of the sequences having sequence identifier, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative member of species to describe the genus. Thus applicant was not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-2, 4-17 and 20-21 are rejected under 35 U.S.C. 102(e) as being anticipated by George-Hyslop, P. H. St. et al. (US Pat. 5986054).

George-Hyslop et al. teach the nucleic acid sequence encoding presenilin 1 (PS1), which is the human homologue or form of *C. elegans Sel*-12 gene (see column 35, lines 29-32, example 5, and SEQ ID NO: 1 that encodes the PS1 polypeptide having SEQ ID NO:2). Thus, George-Hyslop et al. teach a nucleic acid encoding SEL12 protein. in which George-Hyslop's sequence encodes PS1 protein (see the patent claims 1-2), as applied to claims 1-2, 5 and 7-9 of the instant application.

George-Hyslop et al. teach a gene homologous to *Sel*-12, i.e., presenilin genes PS1 and PS2 (see column 3, lines 20-27, and column 35, lines 31-32), as applied to claim 5 of the instant application, and mutants thereof that are generated by mutagenesis (see column 8, line 60-67, column 2, line 52 to column 3, line 8, and columns 20-23, and Tables 7-11), as applied to the application claims 4, 6 and 11.

George-Hyslop et al. teach a mRNA molecule encoding PS1 was isolated using northern blot (see example 7, as applied to claim 10 of the instant application.

George-Hyslop et al. teach that cDNA encoding PS1 was placed in plasmid pCDNA3 which is expressed in a mammalian cell, e.g., CHO cell (see column 56, lines 55-61, column 57, lines 101-11, and Examples 12-13) or plasmid pGEX-kg (see column 52, line 36) expressing in E.coli. (see column 22, lines 63-67), as applied to claims 15-17 and 20-21 of the current application

Because claims 12 sets forth a nucleic acid sequence without reciting a specific SEQ ID NO:_ nor the limitation for the claimed "a unique sequence", and because George-Hyslop et al. teach that the mammalian PS1 gene is an invertebrate homologue, i.e., *C. elegans Sel*-12 gene (see column 35, lines 31-32), the above George-Hyslop et al. teachings meet the limitation of claim 12 and its dependent claims 13-14.

Thus, the above George-Hyslop et al. teachings anticipate claims 1-2, 4-17 and 20-21.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483.

The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

SWL

Samuel Wei Liu, PhD.

July 2, 2002